

Is Sperm Motility Maturation Affected by Static Magnetic Fields?

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Kinematic parameters were evaluated in mouse epididymal extracts to monitor maturation of sperm movement in animals exposed to static magnetic fields using the Sperm-Class Analyzer computerized image analysis system. For this purpose, animals were exposed to a field of 0.7 T generated by a permanent magnet over 10 or 35 days for either 1 or 24 hr/day. The values of the motion endpoints were similar in animals used as controls and in those exposed to the nonionizing radiation, whatever the period of exposure or daily dosage. Changes in motility were observed in all groups: the percentage of total motile and progressive motile spermatozoa increased during passage through the epididymis, with major changes between the caput and corpus epididymides, and the pattern of swimming changed clearly towards more rapid and straighter trajectories. The processes of initiation of sperm motility and maturation of displacement patterns were not then affected by magnetic treatment. Moreover, it appears that sperm production is unaffected because no changes were observed in testicular or epididymal weights after exposure to static magnetic fields. **Key words:** computer-assisted analysis, mice, motility, sperm maturation, static magnetism. *Environ Health Perspect* 104:1212–1216 (1996)

At present, 15% of all couples of reproductive age have difficulty achieving pregnancy (1), and it has been estimated that up to 50% of all fertility problems may be due, directly or indirectly, to male reproductive disorders (2). Recently, Carlsen et al. (3) performed an extensive analysis of historical data on human sperm quality and concluded that seminal plasma volume and sperm concentration had declined significantly between 1940 and 1990. This study has been followed by new reports confirming a deterioration in sperm characteristics, some of them showing a reduction in the percentage of motile and morphologically normal spermatozoa (4,5), as well as a decline in sperm count.

The findings mentioned above have led to much speculation about possible causes of the decline in male fertility. Some man-made substances may interfere with reproductive parameters because they behave like xenoestrogens (6,7), and many other factors such as elevated temperatures [i.e., for ceramists in industry (8)] and changes in life style (9,10) may also contribute, separately or additionally, to the degradation in male reproductive health.

Because of the high mitotic rate of germ cells, the testes are a vulnerable organ when exposed to static or time-varying magnetic fields (11,12). Static magnetic fields (SMF) may be encountered in some occupations in which large direct currents are used (e.g., electrolysis) and in certain new technologies for energy production such as fusion reactors or specialized high energy physics research facilities, where the static magnetic field flux densities in areas accessible to operations personnel may reach 50 mT (13). Members of the general public may also be exposed to static or time-varying

magnetic fields: 1) the application of magnetic field devices is widely used in medicine for various therapeutic applications (14) and for medical diagnosis (15,16) in which stationary magnetic fields with intensities of up to 2 T may be used in the course of an examination (13); 2) magnetically levitated trains can produce magnetic flux at floor level of the passenger compartment of 50–100 mT (13); and 3) very small permanent magnets are encountered even in domestic situations (their influence on human health, if any, has not been studied). Notwithstanding this, the number of studies on the possible relationship between male fertility and magnetic field exposure is very low and experimental outcomes are very different: reversible changes in spermatogenic epithelium (11), aberrations in rat spermatozoa (17,18) beneficial effects on salmon sperm motility (19,20), or no effects on human fertility (21).

As spermatozoa pass through the epididymis after leaving the testis, they experience a series of physiological changes that give them the ability to fertilize eggs. Among these changes, membrane remodeling, progressive compaction of nuclear DNA, and acquisition of capacity for swimming are of great relevance for the spermatozoan function (22). With respect to sperm motility, flagellar beating depends on a fine balance between structural, metabolic, and molecular components involved in the mechanism of sliding between the adjacent outer doublet microtubules mediated by the dynein arms (23,24). Variations induced by magnetic fields in Ca^{2+} flux, for instance, which have been shown to occur in some cells, e.g., T-lymphocytes (25), osteoblasts (26), and nerve

cells (27), could alter this balance and would therefore presumably lead to a detectable change in sperm movement. For this reason, simple evaluation of sperm motility by Computer Assisted Semen Analysis (CASA) systems (28,29) or together with other tests (30,31) is today a widely used practice for the assessment of the effects of toxicants on sperm function because it allows objective data to be obtained and permits the detection of small but significant changes induced in sperm motion (29,30).

In this study, mice were exposed to a constant intensity SMF for different periods of time and dosage, and the process of maturation of sperm motility in the epididymis was monitored with the use of a CASA system.

Materials and Methods

Animal maintenance and dosing protocol.

A total of 30 male albino mice (6 months of age; Of₁ strain; CRIFFA, Barcelona, Spain) was used. Animals were maintained at approximately 25°C and 55% humidity with a 12 hr:12 hr light–dark cycle and had access to standard chow (Letica S.A., Barcelona, Spain) and water *ad libitum*. Throughout the experiments, they were housed individually in plastic boxes placed onto a Terapion plus rectangular magnet (15.5 cm × 10.5 cm, × 3 cm, flux density: 0.7 T; Terapion, Valencia, Spain) for the period of exposure to the generated magnetic field; dosage is shown in Table 1.

Sperm motility assessment. Animals were killed by cervical dislocation and testes and epididymides were quickly excised and weighed. Small segments of the caput, corpus, and cauda of the epididymis (Fig. 1) were placed in centrifuge tubes containing 100 ml of Ham-F10 medium supplemented with 4 mg/ml bovine serum albumin (Fraction V) and 5.7 mg/ml Hepes, pH 7.4. After mincing them separately with iridectomy scissors, 10 min was allowed at 37°C for release of sperm. The tissue was then removed and the sperm suspensions

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diluted with medium to a final concentration of $20\text{--}30 \times 10^6$ spermatozoa/ml. All chemicals were purchased from Sigma Chemical Co., St Louis, MO.

Sperm motion endpoints were measured by means of computer-assisted image analysis using a Sperm-Class Analyzer (SCA; Microptic, Barcelona, Spain). For this purpose, 23 μl of the sperm suspensions was placed on prewarmed siliconized slides and covered with $24 \times 24 \text{ mm}^2$ coverslips to achieve a calculated depth of 40 μm . Slides were examined using an Olympus BHS microscope (Olympus Optical Co., Tokyo, Japan) equipped with a heated stage set at 37°C , a $10\times$ negative phase contrast objective (Olympus A10NH), and a $3.3\times$ photo-ocular interfaced to a Sony CCD AVC-D7CE video camera (Sony Corporation, Tokyo, Japan) and two monitors (Compaq Video Graphics Monitor, Compaq Computer Corporation, Houston, TX, and PVM-1443MD Sony Trinitron, Sony Corporation, Tokyo, Japan). Four to eight fields were recorded onto VHS videotapes for 15 sec/field to permit subsequent analysis of at least 100 spermatozoa from each sample.

With this optical system, the sperm heads appear on the monitor as bright objects on a dark background. The SCA system detected the sperm heads, calculated their centroids, and tracked their changes in position from one video frame to the next. Only objects that were larger in size and higher in luminosity than user-defined threshold values were analyzed. Other instrument settings were frames acquired, 16; acquisition rate, 25 Hz; and minimum number of points per track required for analysis, 6. Among the list of computer-calculated kinematic parameters, we have selected only parameters widely referred to in the related literature and those with demonstrated usefulness in predicting ability of a sperm sample to fertilize: curvilinear velocity (VCL, mean frame-to-frame velocity); straight-line velocity (VSL, velocity between centroids in first and last frame tracked); average path velocity (VAP, velocity of the computer-calculated average trajectory); straightness ($\text{STR} = [\text{VAP}/\text{VCL}] \times 100$); linearity ($\text{LIN} = [\text{VSL}/\text{VCL}] \times 100$); degree

of oscillation of the curvilinear path about its spatial average ($\text{WOB} = [\text{VAP}/\text{VCL}] \times 100$), and amplitude of lateral head displacement (ALH) (see Fig. 2).

The percentage of motile spermatozoa in a sample was determined visually from the videotapes. The total number of sperm in a static visual field was determined using the video pause function. The tape was then allowed to run, and sperm that remained in their original position were counted as immotile or nonprogressing cells, depending on the occurrence of flagellation. At least 200 spermatozoa were counted in each sample.

Statistical analysis. The Kolmogorov-Smirnov test and Bartlett's test were performed to analyze data normality and homogeneity of variances, respectively. If data satisfied these assumptions, full factorial multivariate analysis of variance (MANOVA) was performed, followed by the Scheffé test for group comparisons. Otherwise, the Kruskal-Wallis test was employed. Differences were considered significant at $p < 0.05$.

Results

In all groups, body weight, as well as testicular and epididymal weights, were unaffected by SMF exposure (Table 2). Differences between animals killed after 10

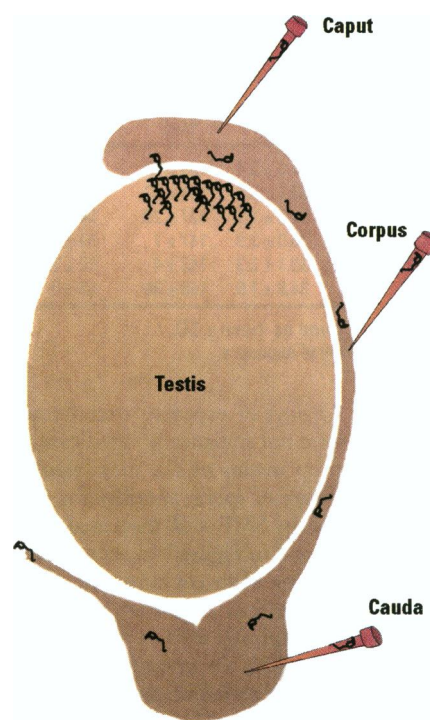


Figure 1. Schematic representation of the murine testis and epididymis indicating the epididymal sites from which spermatozoa were sampled.

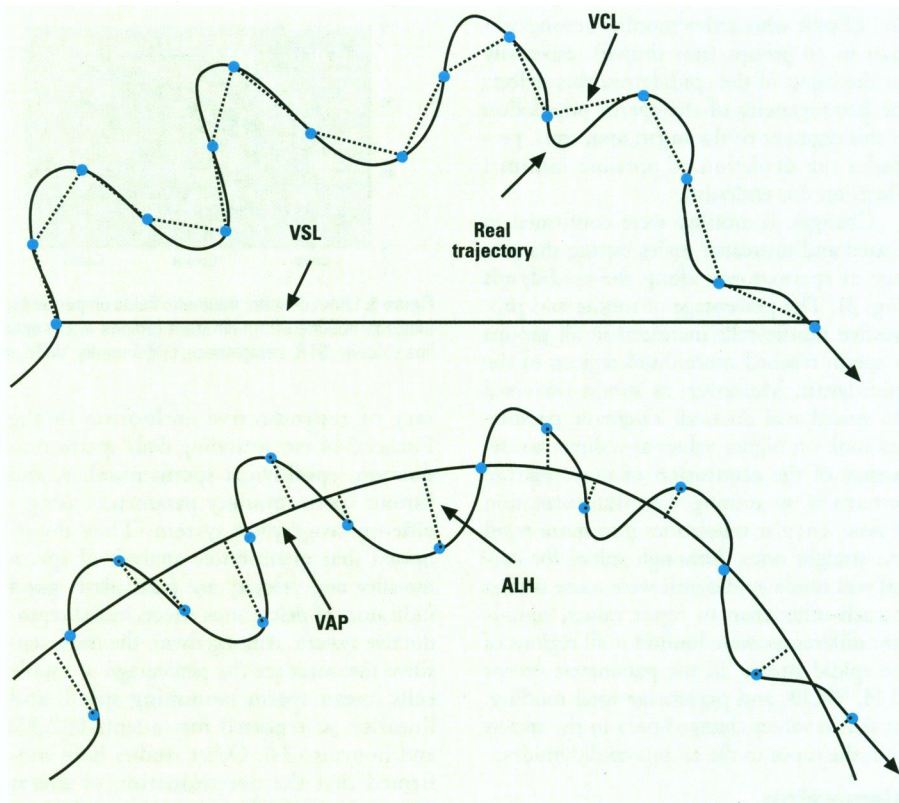


Figure 2. Definition of sperm tracks and related parameters. VCL, curvilinear velocity; VSL, straight-line velocity; VAP, average path velocity; ALH, amplitude of lateral head displacement. The blue circles show the position of the sperm head centroid in each frame.

Table 1. Schedule exposure of mice to a magnetic field of 0.7 T generated by a Terapion plus permanent magnet

Group	n	Exposure period (days)	Dose (hr/day of exposure)
1C (control)	5	10	0
1L (low)	5	10	1
1H (high)	5	10	24
2C (control)	5	35	0
2L (low)	5	35	1
2H (high)	5	35	24

Table 2. Effect of exposure to magnetic fields on reproductive parameters in mice

Exposure period ^a	Body wt. (g)	Testis wt. (mg)	Epididymis wt (mg)
0 (10 days)	37.1 ± 3.4	135 ± 13	56 ± 13
0 (35 days)	36.1 ± 3.8	130 ± 30	54 ± 7
1 (10 days)	38.3 ± 1.9	127 ± 20	54 ± 4
1 (35 days)	36.0 ± 3.9	147 ± 7	54 ± 5
24 (10 days)	39.1 ± 2.3	143 ± 4	62 ± 12
24 (35 days)	34.6 ± 1.6	148 ± 34	53 ± 6

Values are given as mean ± SD.

^aHours per day of exposure

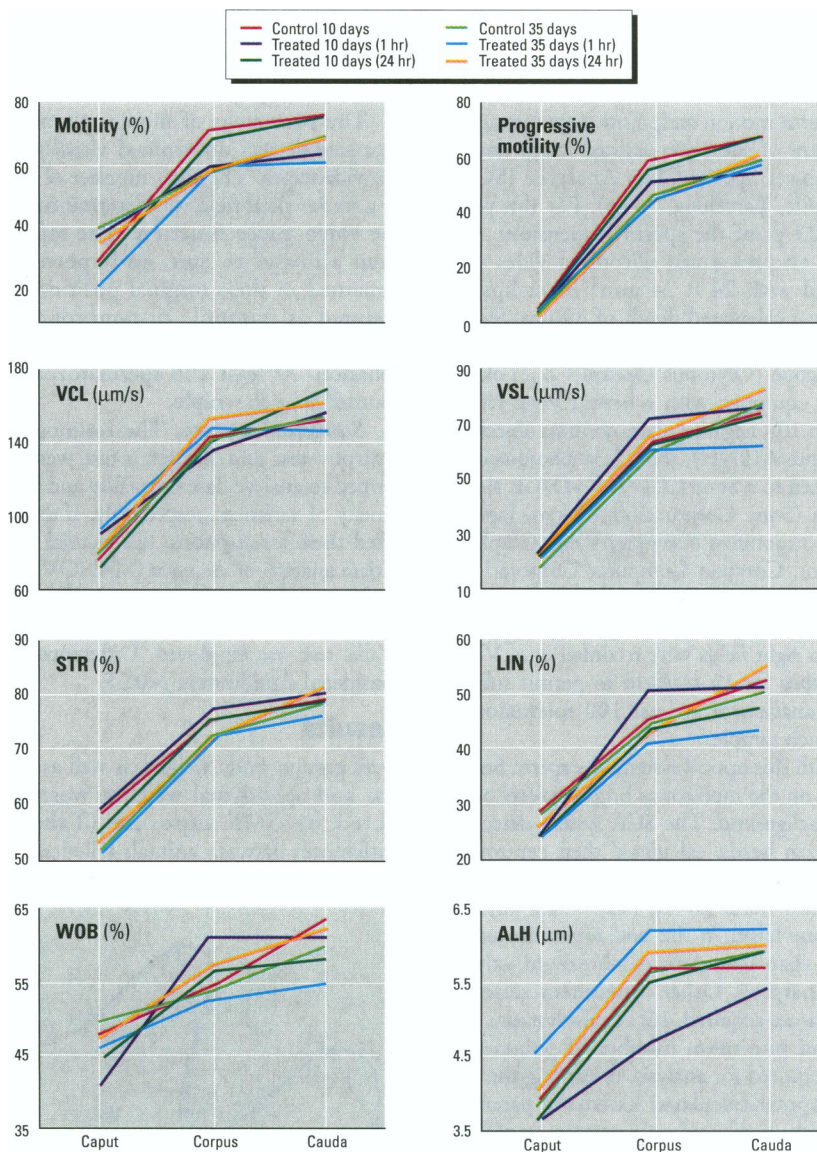
days and 35 days of exposure were found, but these were not statistically significant.

The group means of the most significant parameters of sperm motility for animals exposed to SMF and untreated controls are depicted in Figure 3 to show trends in the maturation of sperm kinematics. The values of the motion endpoints measured were similar in animals used as controls and in those exposed to the constant magnetic flux, whatever the period of exposure (10 or 35 days) or daily dosage (1 or 24 hr). There was also no effect on the process of initiation of sperm motility, as the percentage of motile spermatozoa and progressive motile spermatozoa in treated animals was not statistically different from controls. There was, however, a wide variability in the proportion of cells with active motility among animals in all groups (not shown), especially for the caput of the epididymis; this reflects the heterogeneity of the sperm population in this segment of the organ and, thus, precludes the detection of possible minimal effects on this endpoint.

Changes in motility were confirmed in treated and untreated males during the passage of spermatozoa along the epididymis (Fig. 3). The percentage of motile and progressive motile cells increased in all groups as sperm reached more distal regions of the epididymis. Moreover, as sperm traversed the epididymal duct, all kinematic parameters took on higher values as a direct consequence of the acquisition of more mature patterns of swimming, i.e., transformation of slow, circular trajectories into more rapid and straight ones. Although values for corpus and cauda epididymis were more similar to each other than to caput values, significant differences were found for all regions of the epididymis in all the parameters except ALH, WOB, and percentage total motility, for which values changed only in the transit from the caput to the corpus epididymides.

Discussion

In an effort to determine the most sensitive measures of testicular and epididymal functioning, Blazak et al. (32) examined a bat-

**Figure 3.** Effect of static magnetic fields on percentage motility and six kinematic parameters (ordinate) of spermatozoa obtained from different regions of the epididymis (abscissa). VCL, curvilinear velocity; VSL, straight-line velocity; STR, straightness; LIN, linearity; WOB, wobble; ALH, amplitude of lateral head displacement.

tery of reproductive endpoints in the Fischer 344 rat, including daily sperm production, epididymal sperm number, and various sperm motility parameters using a videomicrographic system. They determined that quantitative analysis of sperm motility and velocity are particularly good indicators of deleterious effects in the reproductive system. Among them, the most sensitive measures are the percentage of motile cells, mean sperm swimming speed, and linearity, as reported for rodents (32,33) and humans (34). Other studies have confirmed that the determination of sperm kinematics by CASA systems is a useful tool in the evaluation of toxicological effects in studies using animal models (29,31).

The kinematics of flagellar bending are

not constant throughout the lifespan of the sperm cells. Mammalian spermatozoa gain the capacity for motility during the transit through the epididymis as its epithelial surfaces and secretions interact with immature spermatozoa arriving from the testis (22,35). As a consequence, sperm cells progressively develop more mature patterns of swimming, which gives them the capacity to move efficiently once in the female genital tract and negotiate the egg membranes during the process of fertilization. These sequential events in the maturation of sperm motility have been clearly shown in mice by using CASA methodology in a fairly recent study (36) and are now confirmed in this paper; the passage of spermatozoa from the caput to the corpus of the

epididymis is the critical period in the acquisition of progressive motility and in the increase in velocity, straightness, and linearity of sperm trajectories.

In so far as the effects of animal exposure to SMF are concerned, within the limitations of the present study, there were no significant differences in the proportion of motile cells or in the values of the parameters characterizing the sperm movement between experimental and control groups in any of the regions of the epididymis studied.

Few data exist concerning the sensitivity of sperm motility to magnetic flux. No variations in the percentage of motile sperm were found in a group of workers exposed to electromagnetic fields (21). On the contrary, an increase in the percentage of activated ejaculated sperm and a prolongation of their viability were shown in fish after *in vitro* sperm exposure to magnetic fields of up to 100 mT (19). An increase in the percentage of successfully fertilized eggs was also demonstrated in a companion paper (20). Nevertheless, substantiation of the current findings for epididymal sperm is not possible because no comparable studies exist; the potential for comparison with the above mentioned reports is, moreover, severely compromised by the use of an alternative methodological approach, including the source of sperm and the greater reliability of our study due to the objectivity conferred by the SCA system. In addition to this, conclusions based on *in vitro* experiments may have limited application to the *in vivo* system.

We found no significant differences in body weight between experimental and control animals. The same result was obtained for mice and rats exposed to fields of up to 0.8 T for up to 250 days (37). However, other reports showed a weight loss after postnatal exposure of mice to SMF (38,39), although this may be due to the fact that at this age the growth rate is more vulnerable.

With regard to epididymal and testicular weights, comparable measures were obtained for exposed and unexposed animals; thus, it appears that sperm production was not affected by SMF and neither was there any epididymal or testicular development or regression. Nevertheless, it is worth mentioning that, although testis weight is recognized to be a sensitive indicator of testicular damage and unless other circumstances are at play to alter it (tumors, edema, inflammation, etc.), there is usually a strong correlation between testis weight and the number of germ cells present in the testis (40). Its validity cannot be stated without reservation because there are several reports in the literature of significant testicular damage that occurs with no change in testis weight (41). On the other

hand, only one paper reported an increase in testis weight resulting from exposure to magnetic fields (42), but the period of exposure (gestation) and the characteristics of the generated flux (time varying) were different from those used in our study. In our laboratory, we are currently investigating the histopathology of the testis in animals exposed prenatally and postnatally to SMF in which initial qualitative examination has shown no evidence of any increase in germ cell degeneration or in the staging of spermatogenesis (unpublished results).

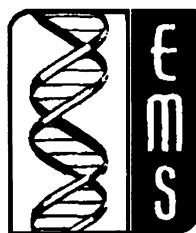
Only a few guidelines limiting patient, device operator, and occupational exposure to static magnetic fields have been developed. In most of the countries in which national protection measures against magnetic fields have been published, exposures of up to 2 T are considered safe, but this is influenced by period of exposure and the region of the body exposed (13). Other recommendations, for example that pregnant women should not be exposed, are generally accepted because the safety of such exposures has not been established. The results presented here do not substantiate theories of deleterious effects to male reproductive health from magnetic fields and, in particular, do not support the view that sperm maturation in the epididymis is adversely affected by static magnetic fields as judged by sperm motility parameters, although we cannot overlook the possibility of magnetic fields having a detrimental effect on other sperm characteristics. In addition to this, we should be careful when extrapolating our results to humans because further development of dosimetric concepts and their theoretical and experimental basis is required in order to guarantee an appropriate formulation of protection standards and exposure limits.

From the methodological point of view, computer-assisted semen analysis appears to facilitate the development of suitable methods for the evaluation of the potential toxicity of radiation in the reproductive system as it offers additional parameters for the characterization and evaluation of spermatozoal motion dynamics and allows for accurate comparisons between laboratories.

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